Disease Pathogenesis

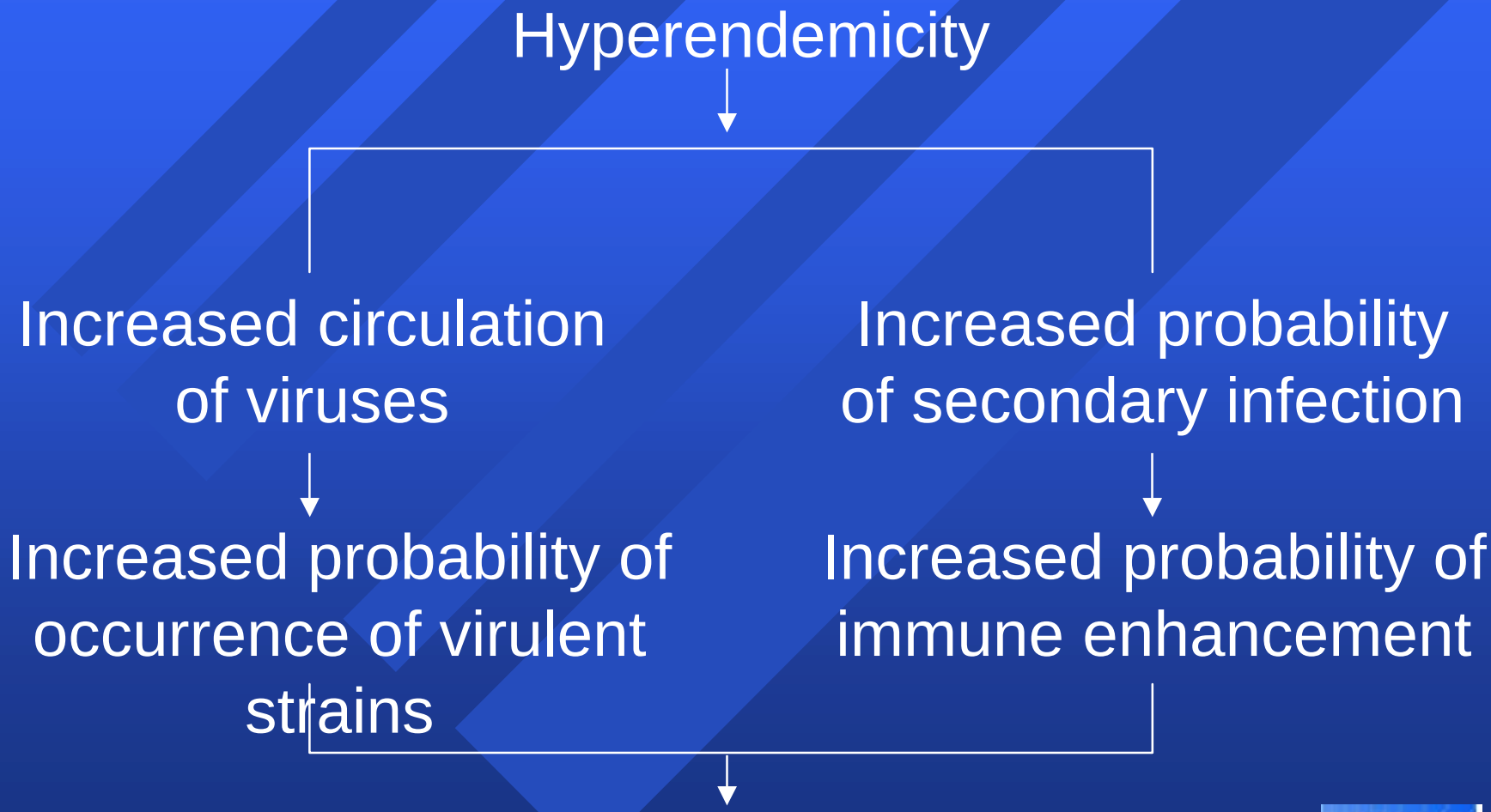
Risk Factors Reported for DHF

- Virus strain
- Pre-existing anti-dengue antibody
  - previous infection
  - maternal antibodies in infants
- Host genetics
- Age

Risk Factors for DHF (continued)

- Higher risk in secondary infections
- Higher risk in locations with two or more serotypes circulating simultaneously at high levels (hyperendemic transmission)

Increased Probability of DHF



Gubler & Trent, 1994

Hypothesis on Pathogenesis of DHF (Part 1)

- Persons who have experienced a dengue infection develop serum antibodies that can neutralize the dengue virus of that same (homologous) serotype

Homologous Antibodies Form Non-infectious Complexes

1 Dengue 1 virus

Neutralizing antibody to Dengue 1 virus

Non-neutralizing antibody

1 Complex formed by neutralizing antibody and virus

CDC

Hypothesis on Pathogenesis of DHF (Part 2)

- In a subsequent infection, the pre-existing heterologous antibodies form complexes with the new infecting virus serotype, but do not neutralize the new virus

Heterologous Antibodies Form Infectious Complexes

2 Dengue 2 virus

Non-neutralizing antibody to Dengue 1 virus

2 Complex formed by non-neutralizing antibody and virus

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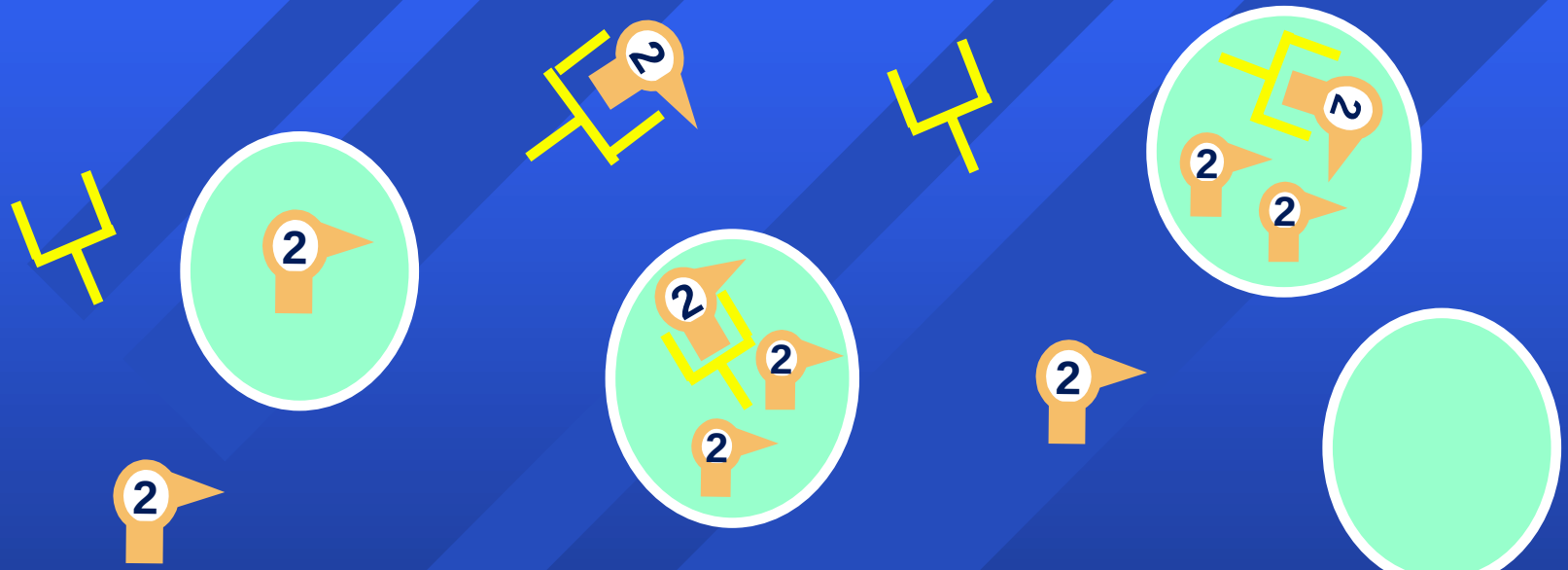
Hypothesis on Pathogenesis of DHF (Part 3)

- Antibody-dependent enhancement is the process in which certain strains of dengue virus, complexed with non-neutralizing antibodies, can enter a greater proportion of cells of the mononuclear lineage, thus increasing virus production

Heterologous Complexes Enter More Monocytes, Where Virus Replicates



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Hypothesis on Pathogenesis of DHF (Part 4)

- Infected monocytes release vasoactive mediators, resulting in increased vascular permeability and hemorrhagic manifestations that characterize DHF and DSS

Viral Risk Factors for DHF Pathogenesis

- Virus strain (genotype)
  - Epidemic potential: viremia level, infectivity
- Virus serotype
  - DHF risk is greatest for DEN-2, followed by DEN-3, DEN-4 and DEN-1

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